

# A Pathway to Clearer Vision

It's something that happens inside every living cell of every creature within the animal and plant kingdoms.

An important alliance occurs between a protein-degrading enzyme, called a proteasome, and a smart, omnipresent protein referred to, not surprisingly, as ubiquitin. Collectively called the "ubiquitin-proteasome pathway," it helps balance the concentration of proteins within cells.

This balance is important because some proteins need to be cleared from the body's cells, for example, after having become oxidized.

ARS-funded biochemists Allen Taylor and Fu Shang have reported findings about the workings of the ubiquitin-proteasome pathway that hold important implications for eye health. Both scientists are with the Laboratory for Nutrition and Vision Research at the Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University in Boston, Massachusetts. Taylor heads the laboratory.

When damaged proteins gather within the eye's lens, cloudiness occurs. These opacities are called cataracts. The protein buildup could also lead to age-related macular degeneration.

Taylor and Shang have found that an accumulation of damaged proteins indicates a breakdown of the protective ubiquitin-proteasome pathway.

## How Does It Work?

Within cells, ubiquitin identifies and attaches to proteins that are ripe for degradation and removal. The resulting "ubiquitin-conjugated proteins" latch onto the proteasome enzyme, which degrades the proteins.

"During the last process of the pathway, the ubiquitin is recycled," says Taylor.

Efficient removal of denatured proteins within the eye lens—or their repair by other proteins—is crucial for maintenance of lens

transparency. When the lens accumulates too many damaged proteins, the resulting cataracts cause blindness.

Taylor, Shang, and colleagues were the first to observe the pathway in cells within the eye's lens, retina, and cornea and have reported those findings in *Experimental Eye Research*, *The Journal of Biological Chemistry*, *Investigative Ophthalmology and Visual Science*, and other journals.

## Obstructing the Pathway

The researchers have also shown that free radicals—highly active molecules that damage cells—actually attack ubiquitin,

other components of the pathway, and other healthy proteins in the eye. Such activity wipes out the benefit-giving pathway.

Free radicals churn in the body as a result of normal metabolism as well as insults such as pollution and ingested toxins (think excessive alcohol or smoke).

"The ubiquitin-proteasome pathway acts as a defense system against oxidative stress," says Shang, "but the pathway itself could be damaged by severe oxidative stress. Antioxidants, such as vitamins C and E, and antioxidant enzymes, such as superoxide dismutase

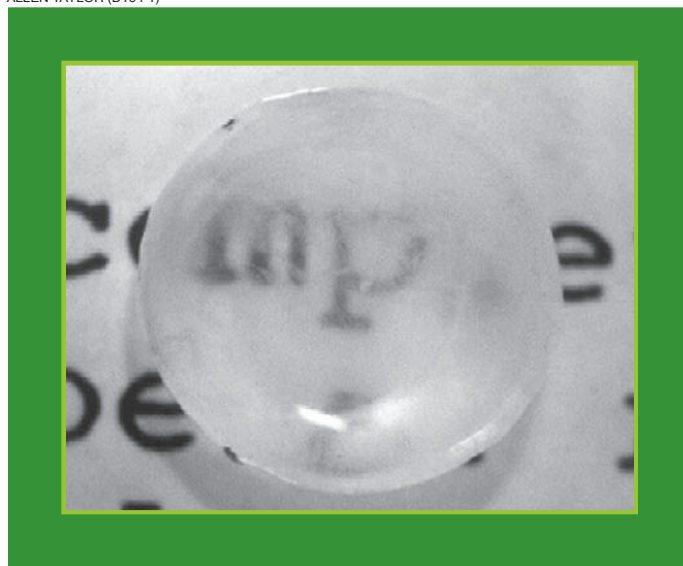
and catalase, may play an important role in protecting the pathway."

Taylor and Shang are now examining ways in which antioxidant nutrients might keep the pathway active longer.—By **Rosalie Marion Bliss**, ARS.

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**A rat's eye lens with a developing cataract.**

Efficient removal of denatured proteins within the **eye lens**—or their repair by other proteins—is crucial for maintenance of lens transparency.